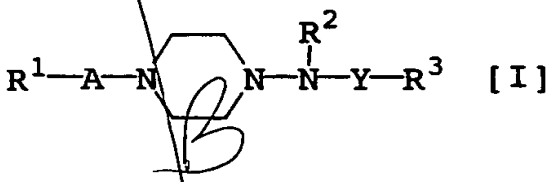
CLAIMS

1. An agent for expression of long-term potentiation of synaptic transmission, which comprises a compound having a brain somatostatin activation property as an active ingredient.

2. The agent for expression of long-term potentiation of synaptic transmission of claim 1, wherein the compound exerts an action to promote a release of brain somatostatin through suppression of a negative feedback mechanism of brain somatostatin release.

3. The agent for expression of long-term potentiation of synaptic transmission of claim 1 or claim 2, wherein the compound has the following formula [I]:



[I]

wherein

R^1 is lower alkyl, aryl, ar(lower)alkoxy or heterocyclic group, each of which may be substituted with halogen,

R^2 is hydrogen atom or lower alkyl,

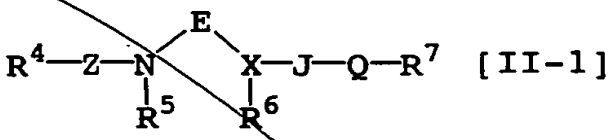
R^3 is cyclo(lower)alkyl, aryl or ar(lower)alkyl, each of which may be substituted with halogen,

A is -CO-, $-SO_2-$ or lower alkylene, and

Y is -CO-, $-SO_2-$ or -CONH-,

or pharmaceutically acceptable salts thereof.

4. The agent for expression of long-term potentiation of synaptic transmission of claim 1 or claim 2, wherein the compound has the following formula [II-1]:



[II-1]

wherein

R^4 is acyl,

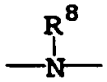
R^7 is lower alkyl, lower alkoxy, lower alkylamino, lower alkenyl, lower alkenyloxy, lower alkenylamino, lower alkynyl, lower alkynyloxy, lower alkynylamino, cyclo(lower)alkyl, cyclo(lower)alkyloxy, cyclo(lower)alkylamino, aryl, aryloxy, arylamino, a heterocyclic group or amino substituted with a heterocyclic group, each of which may be substituted with suitable substituent(s); or acyl;

Z is a single bond, -CO- or $-SO_2-$,

E is lower alkylene optionally substituted with suitable substituent(s),

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl, substituted-lower alkyl, an N-protective group, aryl, acyl or a heterocyclic group,

Q is $-CH_2-$, -CO-, $-SO_2-$ or -N=CH-, and

R^5 and R^6 are each hydrogen or lower alkyl, or are taken together to form lower alkylene optionally condensed with a cyclic hydrocarbon or a heterocyclic ring,

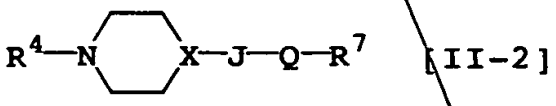
provided that when X is N,

then 1) J is a single bond, and Q is $-CH_2-$, -CO- or $-SO_2-$, or

2) J is lower alkylene,

or pharmaceutically acceptable salts thereof.

5. The agent for expression of long-term potentiation of synaptic transmission of claim 1 or claim 2, wherein the compound has the following formula [II-2]:



[II-2]

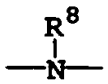
wherein

R^4 is acyl,

R^7 is aryl, aryloxy or arylamino, the aryl moiety of all of which may be substituted with halogen; pyridyl; or pyridylamino;

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl or an N-protective group,

Q is $-CH_2-$, $-CO-$ or $-SO_2-$,

provided that when X is N, then J is a single bond or lower alkylene, or pharmaceutically acceptable salts thereof.

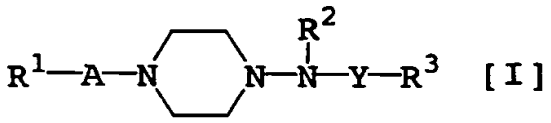
6. The agent for expression of long-term potentiation of synaptic transmission of any of claim 1 to claim 5, which is an agent for the prophylaxis or treatment of cerebral diseases.

7. The agent for expression of long-term potentiation of synaptic transmission of claim 6, which is an agent for the prophylaxis or treatment of dementia or amnesia.

8. A method for expressing long-term potentiation of synaptic transmission, comprising administering an effective amount of a compound having a brain somatostatin activation property.

9. The method for expressing long-term potentiation of synaptic transmission of claim 8, wherein the compound exerts an action to promote a release of brain somatostatin through suppression of a negative feedback mechanism of brain somatostatin release.

10. The method for expressing long-term potentiation of synaptic transmission of claim 8 or claim 9, wherein the compound has the following formula [I]:



[I]

wherein

R^1 is lower alkyl, aryl, ar(lower)alkoxy or heterocyclic group, each of which may be substituted with halogen,

R^2 is hydrogen atom or lower alkyl,

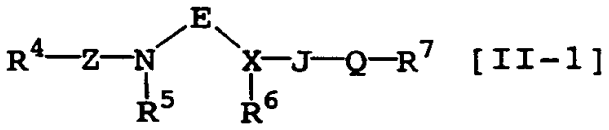
R^3 is cyclo(lower)alkyl, aryl or ar(lower)alkyl, each of which may be substituted with halogen,

A is -CO-, $-SO_2-$ or lower alkylene, and

Y is -CO-, $-SO_2-$ or -CONH-,

or pharmaceutically acceptable salts thereof.

11. The method for expressing long-term potentiation of synaptic transmission of claim 8 or claim 9, wherein the compound has the following formula [II-1]:



[II-1]

wherein

R^4 is acyl,

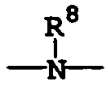
R^7 is lower alkyl, lower alkoxy, lower alkylamino, lower alkenyl, lower alkenyloxy, lower alkenylamino, lower alkynyl, lower alkynyloxy, lower alkynylamino, cyclo(lower)alkyl, cyclo(lower)alkyloxy, cyclo(lower)alkylamino, aryl, aryloxy, arylamino, a heterocyclic group or amino substituted with a heterocyclic group, each of which may be substituted with suitable substituent(s); or acyl;

Z is a single bond, -CO- or $-SO_2-$,

E is lower alkylene optionally substituted with suitable substituent(s),

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl, substituted-lower alkyl, an N-protective group, aryl, acyl or a heterocyclic group,

Q is $-CH_2-$, $-CO-$, $-SO_2-$ or $-N=CH-$, and

R^5 and R^6 are each hydrogen or lower alkyl, or are taken together to form lower alkylene optionally condensed with a cyclic hydrocarbon or a heterocyclic ring,

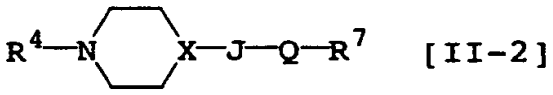
provided that when X is N,

then 1) J is a single bond, and Q is $-CH_2-$, $-CO-$ or $-SO_2-$, or

2) J is lower alkylene,

or pharmaceutically acceptable salts thereof.

12. The method for expressing long-term potentiation of synaptic transmission of claim 8 or claim 9, wherein the compound has the following formula [II-2]:



[II-2]

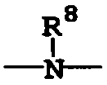
wherein

R^4 is acyl,

R^7 is aryl, aryloxy or arylamino, the aryl moiety of all of which may be substituted with halogen; pyridyl; or pyridylamino;

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl or an N-protective group,

Q is $-CH_2-$, $-CO-$ or $-SO_2-$,

provided that when X is N, then J is a single bond or lower alkylene,

or pharmaceutically acceptable salts thereof.

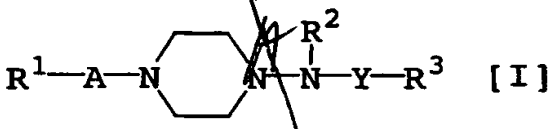
13. The method for expressing long-term potentiation of synaptic transmission of any of claim 8 to claim 12, which is a method for the prophylaxis or treatment of cerebral diseases.

14. The method for expressing long-term potentiation of synaptic transmission of claim 13, which is a method for the prophylaxis and/or treatment of dementia or amnesia.

15. Use of a compound having a brain somatostatin activation property for the production of an agent for the expression of long-term potentiation of synaptic transmission.

16. The use of a compound having a brain somatostatin activation property according to claim 15, wherein the compound exerts an action to promote a release of brain somatostatin through suppression of a negative feedback mechanism of brain somatostatin release.

17. The use of a compound having a brain somatostatin activation property according to claim 15 or claim 16, wherein the compound has the following formula [I]:



[I]

wherein

R^1 is lower alkyl, aryl, ar(lower)alkoxy or heterocyclic group, each of which may be substituted with halogen,

R^2 is hydrogen atom or lower alkyl,

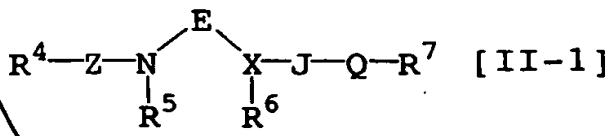
R^3 is cyclo(lower)alkyl, aryl or ar(lower)alkyl, each of which may be substituted with halogen,

A is -CO-, $-SO_2-$ or lower alkylene, and

Y is -CO-, $-SO_2-$ or -CONH-,

or pharmaceutically acceptable salts thereof.

18. The use of a compound having a brain somatostatin activation property according to claim 15 or claim 16, wherein the compound has the following formula [II-1]:



[II-1]

wherein

R^4 is acyl,

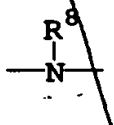
R^7 is lower alkyl, lower alkoxy, lower alkylamino, lower alkenyl, lower alkenyloxy, lower alkenylamino, lower alkynyl, lower alkynyloxy, lower alkynylamino, cyclo(lower)alkyl, cyclo(lower)alkyloxy, cyclo(lower)alkylamino, aryl, aryloxy, arylamino, a heterocyclic group or amino substituted with a heterocyclic group, each of which may be substituted with suitable substituent(s); or acyl;

Z is a single bond, -CO- or $-SO_2-$,

E is lower alkylene optionally substituted with suitable substituent(s),

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl, substituted-lower alkyl, an N-protective group, aryl, acyl or a heterocyclic group,

Q is $-CH_2-$, -CO-, $-SO_2-$ or -N=CH-, and

R^5 and R^6 are each hydrogen or lower alkyl, or are taken together to form lower alkylene optionally condensed with a cyclic hydrocarbon or a heterocyclic ring,

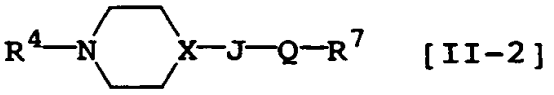
provided that when X is N,

then 1) J is a single bond, and Q is $-CH_2-$, -CO- or $-SO_2-$, or

2) J is lower alkylene,

or pharmaceutically acceptable salts thereof.

19. The use of a compound having a brain somatostatin activation property according to claim 15 or claim 16, wherein the compound has the following formula [II-2]:



[II-2]

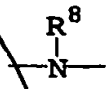
wherein

R^4 is acyl,

R^7 is aryl, aryloxy or arylamino, the aryl moiety of all of which may be substituted with halogen; pyridyl; or pyridylamino;

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl or an N-protective group,

Q is $-CH_2-$, $-CO-$ or $-SO_2-$,

provided that when X is N, then J is a single bond or lower alkylene, or pharmaceutically acceptable salts thereof.

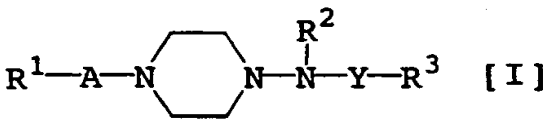
20. The use of a compound having a brain somatostatin activation property according to any of claim 15 to claim 19, which is for the production of an agent for the prophylaxis and/or treatment of cerebral diseases.

21. The use of a compound having a brain somatostatin activation property according to claim 20, which is for the production of an agent for the prophylaxis and/or treatment of dementia or amnesia.

22. A pharmaceutical composition for expression of long-term potentiation of synaptic transmission, which comprises a compound having a brain somatostatin activation property, and a pharmaceutically acceptable carrier or excipient.

23. The pharmaceutical composition for expression of long-term potentiation of synaptic transmission of claim 22, wherein the compound exerts an action to promote a release of brain somatostatin through suppression of a negative feedback mechanism of brain somatostatin release.

24. The pharmaceutical composition for expression of long-term potentiation of synaptic transmission of claim 22 or claim 23, wherein the compound has the following formula [I]:



[I]

wherein

R^1 is lower alkyl, aryl, ar(lower)alkoxy or heterocyclic group, each of which may be substituted with halogen,

R^2 is hydrogen atom or lower alkyl,

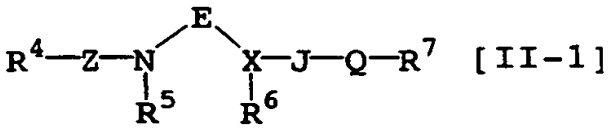
R^3 is cyclo(lower)alkyl, aryl or ar(lower)alkyl, each of which may be substituted with halogen,

A is -CO-, $-SO_2-$ or lower alkylene, and

Y is -CO-, $-SO_2-$ or -CONH-,

or pharmaceutically acceptable salts thereof.

25. The pharmaceutical composition for expression of long-term potentiation of synaptic transmission of claim 22 or claim 23, wherein the compound has the following formula [II-1]:



[II-1]

wherein

R^4 is acyl,

R^7 is lower alkyl, lower alkoxy, lower alkylamino, lower alkenyl, lower alkenyloxy, lower alkenylamino, lower alkynyl, lower alkynyloxy, lower alkynylamino,

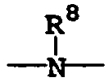
cyclo(lower)alkyl, cyclo(lower)alkyloxy, cyclo(lower)alkylamino, aryl, aryloxy, arylamino, a heterocyclic group or amino substituted with a heterocyclic group, each of which may be substituted with suitable substituent(s); or acyl;

Z is a single bond, -CO- or $-SO_2-$,

E is lower alkylene optionally substituted with suitable substituent(s),

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl, substituted-lower alkyl, an N-protective group, aryl, acyl or a heterocyclic group,

Q is $-CH_2-$, -CO-, $-SO_2-$ or -N=CH-, and

R^5 and R^6 are each hydrogen or lower alkyl, or are taken together to form lower alkylene optionally condensed with a cyclic hydrocarbon or a heterocyclic ring,

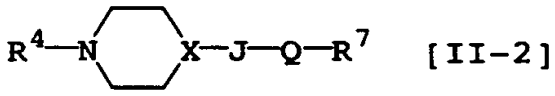
provided that when X is N,

then 1) J is a single bond, and Q is $-CH_2-$, -CO- or $-SO_2-$, or

2) J is lower alkylene,

or pharmaceutically acceptable salts thereof.

26. The pharmaceutical composition for expression of long-term potentiation of synaptic transmission of claim 22 or claim 23, wherein the compound has the following formula [II-2]:



[II-2]

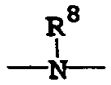
wherein

R^4 is acyl,

R^7 is aryl, aryloxy or arylamino, the aryl moiety of all of which may be substituted with halogen; pyridyl; or pyridylamino;

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl or an N-protective group,

Q is $-CH_2-$, $-CO-$ or $-SO_2-$,

provided that when X is N, then J is a single bond or lower alkylene, or pharmaceutically acceptable salts thereof.

27. The pharmaceutical composition for expression of long-term potentiation of synaptic transmission of any of claim 22 to claim 26, which is a pharmaceutical composition for the prophylaxis or treatment of cerebral diseases.

28. The pharmaceutical composition for expression of long-term potentiation of synaptic transmission of claim 27, which is a pharmaceutical composition for the prophylaxis or treatment of dementia or amnesia.

29. A method for screening an agent for expression of long-term potentiation of synaptic transmission, which comprises using a somatostatin releasing action as an index.

30. The screening method of claim 29, which is a screening method of an anti-dementia agent or anti-amnesia agent.

31. A method for screening an agent for expression of long-term potentiation of synaptic transmission, which comprises stimulating hippocampal slices, bringing a hippocampal slice into contact with a test compound, measuring an amount of somatostatin released from the hippocampal slice and/or a release time thereof, measuring an amount of somatostatin released from a hippocampal slice and/or a release time thereof in the absence of a contact with the test compound, and comparing the amounts and/or the times to calculate the amount of somatostatin released from the hippocampal slice and/or the release

time thereof caused by the contact with the test compound.

32. The screening method according to claim 31, which is a screening method of an anti-dementia agent or anti-amnesia agent.

33. The agent for expression of long-term potentiation of synaptic transmission of claim 1, wherein the compound having the brain somatostatin activation property is a compound obtained by the screening method of any of claim 29 to claim 32.

34. The method for expressing long-term potentiation of synaptic transmission according to claim 8, wherein the compound having the brain somatostatin activation property is a compound obtained by the screening method of any of claim 29 to claim 32.

35. The use of a compound having a brain somatostatin activation property according to claim 15, wherein the compound having the brain somatostatin activation property is obtained by the screening method of any of claim 29 to claim 32.

36. The pharmaceutical composition for expression of long-term potentiation of synaptic transmission of claim 22, wherein the compound having the brain somatostatin activation property is a compound obtained by the screening method of any of claim 29 to claim 32.

37. A commercial package comprising the pharmaceutical composition for expression of long-term potentiation of synaptic transmission of any of claim 22 to claim 28 or claim 36 and a written matter associated therewith, wherein the written matter states that the pharmaceutical composition can or should be used for expression of long-term potentiation of synaptic transmission.

38. A compound selected by the screening method described in any of claim 29 to claim 32.